REMARKS

Applicants respectfully request reconsideration and withdrawal of the outstanding Office Action rejection in view of the foregoing amendments and following remarks. Claims 1 and 2 have been amended to limit the cytokine administered to interferons. No new matter has been added.

Claims 1, 2, 4, 8-10, 12 and 14-17 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Bleumer et al. (January 2002, European Urology Supplements, Vol. 1, No. 1, pp. 112) in view of Pavone et al. (2001, Cancer Immonol. Immunother. 50:82-86). Applicants respectfully submit that the Examiner has not provided adequate motivation to establish a primia facie case of obviousness.

The Examiner contends, at page 5 of the Office Action, that it would have flowed logically from the individual disclosures of Bleumer and Pavone to arrive at a combined, simultaneous treatment for renal cell carcinoma (RCC) comprising a G250 antibody together with interferon-α. The Examiner further contends that a skilled artisan would have an expectation of success because each of a G250 antibody and interferon-α were disclosed as efficacious after individually being administered for treatment of RCC. Applicants respectfully disagree for the following reasons.

The Examiner states at page 5 of the Office Action that a skilled artisan would have been motivated to combine the disclosures because of the known intractability of RCC to therapy. Along these lines, Pavone discloses as the first sentence in the Introduction section that "there is no standard treatment for advanced renal cell carcinoma." Moreover, in the practice of medicine, and particularly in the practice of cancer treatment, it is common to sequentially administer different medications (as

described in Bleumer) because if a first administered medication is found to not be efficacious, a second medication is administered. Since it is known to a skilled artisan that RCC is difficult to treat, it is not uncommon for publications directed to treating RCC to disclose the sequential administration of different medications. In other words, and with respect to treatment of RCC, a skilled artisan interprets sequential administration of medications to mean the first administered medication was found to not be efficacious.

Bleumer discloses a monotherapy for treating RCC using the G250 antibody. From the overall disclosure of Bleumer, a skilled artisan would recognize the treatment of RCC with the G250 antibody as a "second-line" treatment, meaning that the group of 22 patients who received a first treatment of either interferon-α or interleukin-2 were progressive afterwards because the treatment of RCC with either interferon-α or interleukin-2 was found to not be efficacious. Otherwise, the patients would not have needed a further, and different, treatment.

Thus, Applicants submit that a skilled artisan who read the disclosure of Bleumer would be lead away from arriving at a combined, simultaneous treatment of interferon-α and a G250 antibody, as required by the present claims, because a skilled artisan would recognize that the first administered medication of Bleumer (interferon-α) was found to not be efficacious. Furthermore, Bleumer does not provide any details regarding the dosing regimen of interferon-α and a skilled artisan would not be able to derive any dosing information (i.e., high-dose, low-dose) with respect to interferon-α. A skilled artisan who wished to treat RCC would recognize dependence between dosing regimen and efficaciousness.

Pavone discloses using low-dose recombinant interferon-α and interleukin-2 for treating RCC. Pavone is silent with respect to the co-administration of *only one of* interferon-α *or* interleukin-2 with an anti-tumor antibody directed against the MN antigen. Moreover, Pavone does not teach or suggest the use of an anti-tumor antibody or an anti-tumor antibody directed against the MN antigen for treating RCC. A skilled artisan who read the disclosure of Pavone would recognize that the efficaciousness reported therein for treatment of RCC is dependent upon the co-administration of *both* interferon-α *and* interleukin-2. A skilled artisan would have no way of knowing whether or not interferon-α or interleukin-2 would be efficacious as a monotherapy, as there is no such disclosure in Pavone. Accordingly, Applicants submit that a skilled artisan would not have an expectation of success with respect to the efficaciousness of *one, and only one, of* interferon-α *or* interleukin-2 for treatment of RCC.

Thus, Applicants respectfully submit that it would not have been obvious for a skilled artisan to combine the disclosures of Bleumer and Pavone to arrive at the combined, simultaneous treatment required by the present claims because a skilled artisan is aware of the intractability of RCC to therapy and that a skilled artisan would not have expected interferon-α to be efficacious in treating RCC. For at least these reasons, Applicants respectfully request reconsideration and withdrawal of the outstanding Office Action rejection.

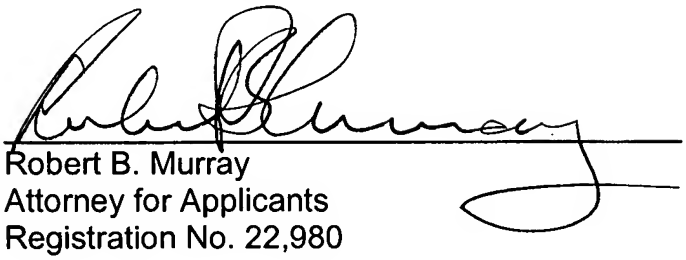
Applicants respectfully point the Examiner's attention to page 1, lines 21-31, of the present specification, wherein it is stated: "To date chemotherapy has not demonstrated sufficient anti-tumor activity to prolong the survival of patients with metastatic disease. *Single agent or multiple agent chemotherapy has not demonstrated*

a response rate greater than 10-15%. Due to less than satisfactory responses to chemotherapy and surgery, and to the indirect evidence that host immune mechanisms play a significant role in the natural history of RCC, there is a continued exploration of immunotherapy in this disease. Interferon-α and interleukin-2 have indeed shown anti-tumor activity in approx. 20% of patients, but this was often associated with severe toxicity."

The inventors of the subject matter of the present application have found that co-administration of a G250 antibody with interferon-α leads to at least a 15% increase in therapeutic efficacy when compared to administration of either a G250 antibody or interferon-α alone, along with a reduction of side effects of such an administration of a chemotherapeutic regimen (please see page 4, line 29 – page 5, line 7 of the present specification). Applicants submit that the at least 15% increase in efficacy stems from a synergistic effect from co-administration of a G250 antibody with interferon-α to treat RCC. Applicants further submit that the co-administration of a G250 antibody with interferon-α represents a clear technical advantage over both Bleumer and Pavone.

In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the outstanding Office Action rejection. Early and favorable action is awaited.

Respectfully submitted,

By 

Robert B. Murray
Attorney for Applicants
Registration No. 22,980

Donald V. Scaltrito, Ph.D.
Patent Agent for Applicants
Registration No. 59,985

ROTHWELL, FIGG, ERNST & MANBECK, P.C.
Suite 800, 1425 K Street, N.W.
Washington, D.C. 20005
Telephone: (202)783-6040

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